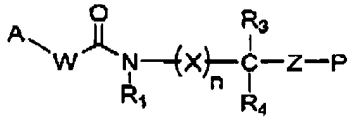
Application No.: 10/001945 Docket No.: PPI-106CP2

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions of the claims and listing of the claims in the application:

1. (Currently Amended) A compound of Formula I,



(I)

wherein

A is a Met-AP2 inhibitory core;

W is O or NR_2;

R_1 and R_2 are each, independently, hydrogen or alkyl;

X is alkylene or substituted alkylene;

n is 0 or 1;

R_3 and R_4 are each, independently, substituted alkyl, substituted aryl or substituted or unsubstituted heteroaryl; or R_3 and R_4, together with the carbon atom to which they are attached, form a carbocyclic or heterocyclic group; or R_3 and R_4 together form an alkylene group;

Z is -C(O)-, alkylene or alkylene-C(O)-; and

P is a peptide comprising from 1 to about 100 amino acid residues attached at its amino terminus to Z or a group OR_5 or $N(R_6)R_7$, wherein

R_5, R_6 and R_7 are each, independently, hydrogen, alkyl, substituted alkyl, azacycloalkyl or substituted azacycloalkyl; or R_6 and R_7, together with the nitrogen atom to which they are attached, form a substituted or unsubstituted heterocyclic ring structure;

or

Z is -O-, $-NR_8$-, alkylene-O- or alkylene-NR_8-, where R_8 is hydrogen or alkyl; and

P is hydrogen or a peptide consisting of from 1 to about 100 amino acid residues attached at its carboxy terminus to Z; wherein

the N-terminus of the peptide is ~~$-NR_2R_3$~~ $-NR_2'R_3'$ wherein ~~R_2~~-R_2' is hydrogen, alkyl or arylalkyl and ~~R_3~~ R_3' is hydrogen, alkyl, arylalkyl or acyl.

2. (Currently Amended) The compound of claim 1, wherein at least one of ~~R_1,~~ R_3 and R_4 is a substituted ~~or unsubstituted~~ alkyl group.

3. (Currently Amended) The compound of claim 2, wherein at least one of ~~R_1,~~ R_3 and R_4 is a substituted ~~or unsubstituted~~ normal, branched or cyclic C_1-C_6 alkyl group.

4. (Currently Amended) The compound of claim 3, wherein at least one of ~~R_1,~~ R_3 and R_4 is a substituted normal or branched C_1-C_4 alkyl group.

5. (Currently Amended) The compound of claim 1, wherein one of R_3 and R_4 is a substituted ~~or unsubstituted~~ aryl group, a substituted or unsubstituted heteroaryl group, or a substituted or unsubstituted heteroarylalkyl group~~, or a substituted or unsubstituted aryl-alkyl group~~.

6. (Currently Amended) The compound of claim 5, wherein one of R_3 and R_4 is selected from the group consisting of ~~phenyl, naphthyl,~~ indolyl, imidazolyl, pyridyl, ~~benzyl, naphthylmethyl~~, indolylmethyl, imidazolylmethyl and pyridylmethyl.

7. (Original) The compound of claim 1, wherein n is 1 and X is C_1-C_6-alkylene.

8. (Original) The compound of claim 7, wherein X is methylene or ethylene.

9. (Original) The compound of claim 1, wherein Z is C_1-C_6-alkylene-C(O)-.

10. (Original) The compound of claim 9, wherein Z is methylene-C(O)- or ethylene-C(O)-.

11. (Previously Presented) The compound of claim 1, wherein at least one of R_6 and R_7 is alkyl, substituted alkyl, substituted or unsubstituted azacycloalkyl or substituted or unsubstituted azacycloalkylalkyl.

12. (Original) The compound of claim 11, wherein at least one of R_6 and R_7 is an azacycloalkyl group having an N-alkyl substituent.

13. (Original) The compound of claim 12, wherein the N-alkyl substituent is a C_1-C_4-alkyl group.

14. (Original) The compound of claim 13, wherein the N-alkyl substituent is a methyl group.

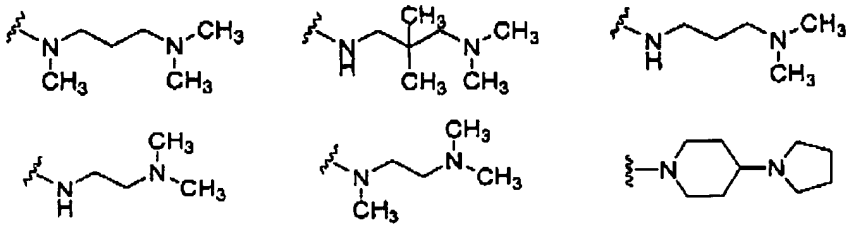
15. (Original) The compound of claim 1, wherein R_6 and R_7, together with the nitrogen atom to which they are attached, form a substituted or unsubstituted five or six-membered aza- or diazacycloalkyl group.

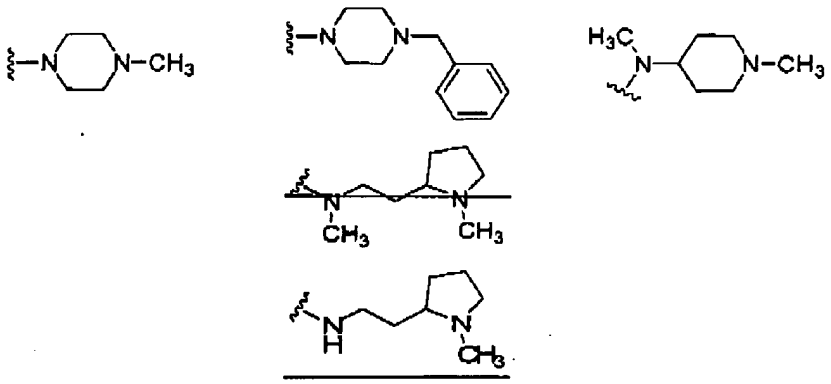
16. (Original) The compound of claim 15, wherein R_6 and R_7, together with the nitrogen atom to which they are attached, form a substituted or unsubstituted five or six-membered diazacycloalkyl group which includes an N-alkyl substituent.

17. (Original) The compound of claim 16, wherein the N-alkyl substituent is a C_1-C_4-alkyl group.

18. (Original) The compound of claim 17, wherein the N-alkyl substituent is a methyl group.

19. (Currently Amended) The compound of claim 1, wherein P is NH_2 or one of the groups shown below:





20.-56. (Cancelled)

57. (Currently Amended) An angiogenesis inhibitor compound selected from the group consisting of

~~N-Carbamoyl-GlyArgGlyAspSerPro-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2R,3R)-2-methyl-3-(3-methyl-butyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;~~

~~N-Carbamoyl-GlyArgGlyAspTyr(OMe)ArgGlu-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2R,3R)-2-methyl-3-(3-methyl-butyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;~~

~~N-Carbamoyl-GlyArgGlyAsp-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2R,3R)-2-methyl-3-(3-methyl-butyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;~~

~~N-Carbamoyl-GlyArgGlyAsp-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2R,3R)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;~~

~~N-Carbamoyl-GlyArg-{3-amino-3(pyridyl)}-propionic acid-(3*R*, 4*S*, 5*S*, 6*R*)-5-methoxy-4-[(2R,3R)-2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;~~

~~N-Carbomoyl-GlyProLeuGly (3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R) 2-methyl-3-(3-methyl-but-2-enyl) oxiranyl] 1-oxa-spiro[2.5]oct-6-yl ester;~~

~~Ac-ProLeuMetTrpAla (2*R*-[(3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R) 2-methyl-3-(3-methyl-but-2-enyl) oxiranyl] 1-oxa-spiro[2.5]oct-6-yloxycarbonyl}-amino-3-methyl-butanol) ester;~~

~~Ac-ProLeuGlyMet (2*R*-[(3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R) 2-methyl-3-(3-methyl-but-2-enyl) oxiranyl] 1-oxa-spiro[2.5]oct-6-yloxycarbonyl}-amino-3-methyl-butanol) ester;~~

~~Ac-ProLeuGlyMetAla 2*R*-[(3*R*, 4*S*, 5*S*, 6*R*) 5-methoxy-4-[(2R,3R) 2-methyl-3-(3-methyl-but-2-enyl) oxiranyl] 1-oxa-spiro[2.5]oct-6-yloxycarbonyl}-amino-3-methyl-butanol) ester;~~

{2-Methyl-1-[methyl-(1-methyl-piperidin-4-yl)-carbamoyl]-propyl}-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

[1-(2-Dimethylamino-ethylcarbamoyl)-2-methyl-propyl]-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

{1-[(2-Dimethylamino-ethyl)-methyl-carbamoyl]-2-methyl-propyl}-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

[1-(3-Dimethylamino-propylcarbamoyl)-2-methyl-propyl]-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

[1-(3-Dimethylamino-2,2-dimethyl-propylcarbamoyl)-2-methyl-propyl]-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

[2-Methyl-1-(4-methyl-piperazine-1-carbonyl)-propyl]-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

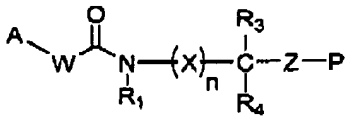
{2-Methyl-1-[2-(1-methyl-pyrrolidin-2-yl)-ethylcarbamoyl]-propyl}-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester;

[2-Methyl-1-(4-pyrrolidin-1-yl-piperidine-1-carbonyl)-propyl]-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester; and

[1-(4-Benzyl-piperazine-1-carbonyl)-2-methyl-propyl]-carbamic acid 5-methoxy-4-[2-methyl-3-(3-methyl-but-2-enyl)-oxiranyl]-1-oxa-spiro[2.5]oct-6-yl ester.

58.-61. (Cancelled)

62. (Currently Amended) A method of treating an angiogenic disease in a subject, comprising administering to the subject a therapeutically effective amount of an angiogenesis inhibitor compound comprising the structure



wherein

A is a Met-AP2 inhibitory core;

W is O or NR_2;

R_1 and R_2 are each, independently, hydrogen or alkyl;

X is alkylene or substituted alkylene;

n is 0 or 1;

R_3 and R_4 are each, independently, ~~hydrogen,~~ substituted ~~or unsubstituted~~ alkyl, substituted ~~or unsubstituted~~ aryl or substituted or unsubstituted heteroaryl; or R_3 and R_4, together with the carbon atom to which they are attached, form a carbocyclic or heterocyclic group; or R_3 and R_4 together form an alkylene group;

Z is -C(O)-, alkylene or alkylene-C(O)-; and

P is a peptide comprising from 1 to about 100 amino acid residues attached at its amino terminus to Z or a group OR_5 or $N(R_6)R_7$, wherein

R_5, R_6 and R_7 are each, independently, hydrogen, alkyl, substituted alkyl, azacycloalkyl or substituted azacycloalkyl; or R_6 and R_7, together with the nitrogen atom to which they are attached, form a substituted or unsubstituted heterocyclic ring structure;
or
Z is -O-, -NR_8-, alkylene-O- or alkylene-NR_8-, where R_8 is hydrogen or alkyl; and
P is hydrogen or a peptide consisting of from 1 to about 100 amino acid residues attached at its carboxy terminus to Z; wherein
the N-terminus of the peptide is $-NR_{2'}R_{3'}$ wherein $R_{2'}$ is hydrogen, alkyl or arylalkyl and $R_{3'}$ is hydrogen, alkyl, arylalkyl or acyl.

63. (Original) The method of claim 62, wherein said angiogenic disease is an autoimmune disease.

64. (Original) The method of claim 63, wherein said autoimmune disease is rheumatoid arthritis.

65. (Original) The method of claim 62, wherein said angiogenic disease is cancer.

66. (Non-Entered Claim) The compound of claim 1, wherein R_1 is a substituted or unsubstituted alkyl group.

67. (Non-Entered Claim) The compound of claim 66, wherein R_1 is a substituted or unsubstituted normal, branched or cyclic C_1-C_6 alkyl group.

68. (Non-Entered Claim) The compound of claim 67, wherein R_1 is a normal or branched C_1-C_4 alkyl group.

69. (New) The compound of claim 1, wherein R_1 is a substituted or unsubstituted alkyl group.

70. (New) The compound of claim 69, wherein R_1 is a substituted or unsubstituted normal, branched or cyclic C_1-C_6 alkyl group.

71. (New) The compound of claim 70, wherein R_1 is a normal or branched C_1-C_4 alkyl group.